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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
09/113,924	07/09/98	BRIGSTOCK	D 08766/003002

EXAMINER

HM12/0330

LISA A HAILE
GRAY CARY WARE AND FREIDENRICH LLP
4365 EXECUTIVE DRIVE, SUITE 1600
SAN DIEGO CA 92121-2189

SPECTOR, L

ART UNIT	PAPER NUMBER
1646	11

DATE MAILED: 03/30/00

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 2/2/00

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-7 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☐ Claim(s) _____ is/are rejected.
☐ Claim(s) _____ is/are objected to.
☒ Claim(s) 1-7 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

Part III: Detailed Office Action

Claims 1-3 and newly introduced claims 4-7 are pending and under consideration.

Formal Matters:

The amended title of the invention is acknowledged.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 7 is rejected under 35 U.S.C. 112,. second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is indefinite because an antibody cannot be an antibody fragment. The whole cannot be a fragment of itself.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no support in the specification as originally filed for an actual human antibody which is reactive with HBGF. The portion of the specification to which applicants have pointed for support of claim 4 discusses only "human" (parentheses included in original text) antibodies, which

are defined therein as "*de novo* antibodies with human constant region sequences", which is the same thing as a 'humanized' antibody. However, such would not be considered by one of ordinary skill in the art to be an actual human antibody, which is generally accepted as being an antibody which has been obtained from a human.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 remain rejected under 35 U.S.C. 102(b) as being anticipated by Grotendorst et al., U.S. Patent Number 5,408,040 for reasons cited in the previous Office Action, paper number 7 mailed 9/29/99, at page(s) 3. Applicants argument that Grotendorst fails to disclose each and every element of the claimed invention has been fully considered but is not deemed persuasive. It is true that Grotendorst did not appreciate that the C-terminal portion of CTGF independently has biological activity, herein referred to as HBGF activity. However, as previously stated, Grotendorst teaches antibodies which specifically bind to CTGF, but not to PDGF; see claims 2-4. By applicants admission at page 14 of the instant specification, HBGF would reasonably be expected to be cross-reactive with anti-CTGF antibodies. Applicants have not contested this point. While one would not necessarily expect *all* anti-CTGF antibodies to cross-react with HBGF, as HBGF is apparently a fragment of CTGF, one of ordinary skill in the art would nonetheless reasonably expect a reasonable number of anti-CTGF antibodies to react with HBGF. Applicants have not contested this point. Further, this is not a case wherein applicants have identified a small portion of the CTGF molecule and are claiming antibodies specifically reactive with that portion; rather, HBGF as disclosed herein

comprises a full 29% of the CTGF sequence, and accordingly, approximately **one third** of Grotendorst's antibodies would fall within the metes and bounds of the instant claims. It is not necessary that each and every antibody disclosed by Grotendorst be within the metes and bounds of the instant claims. The expectation that such a large proportion of Grotendorst's antibodies would meet the limitations of the claims, in the absence of any disclosure of special or unexpected features of the claimed antibodies (e.g. neutralization of HBGF activity, which could not have been anticipated by Grotendorst, but which may not be supported by the instant specification (this is not an invitation to amend the claims)), supports the finding of anticipation. It is not necessary that Grotendorst have appreciated that a fragment of CTGF have its own activity; the fact remains that the claimed antibodies bind to the same sequence to which approximately one third of the antibodies disclosed and claimed by Grotendorst bind. Accordingly, the instant claims appear to be anticipated by the antibodies disclosed and claimed by Grotendorst.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grotendorst et al., U.S. Patent Number 5,408,040 in view of U.S. Patent Number 5,565,332 (Hoogenboom et al.) in the case of claims 6 and 7, or in view of U.S. Patent Number 4,946,778 (Ladner et al.) in the case

of claims 5 and 6.

The teachings of Grotendorst are summarized above. Grotendorst does not teach single chain humanized, or fragment antibodies.

Hoogenboom et al. disclose humanized antibodies and methods of making such. At col. 1 lines 16-30 they disclose the advantages of such as being overcoming the problem of elicitation of anti-globulin response when a non-human antibody is administered to a human. See also col. 3 lines 8-15 in this regard. At column 2 lines 57+, they disclose that antibody fragments can perform the function of whole antibodies, and set forth single chain antibodies as being examples of antibody fragments.

Ladner et al. teach the construction of single chain antibodies . The stated advantages of such as enumerated at column 3 lines 32-48 include smaller size, greater stability, lower cost, lower immunogenicity, etc.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute the anti-CTGF antibodies of Grotendorst et al. into the single chain or humanized antibodies of Ladner et al. or Hoogenboom et al. to attain the known and expected advantages of such as set forth by the secondary references and as referred to above. It is noted that a single chain antibody is considered additionally to be an 'antibody fragment', as disclosed by Hoogenboom et al.

Advisory Information:

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the

THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

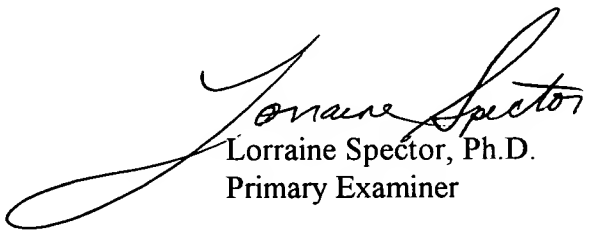
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 8:00 A.M. to 4:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Paula Hutzell, Ph.D, can be reached at (703)308-4310.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 305-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. **Please** advise the Examiner at the telephone number above when an informal fax is being transmitted.



Lorraine Spector, Ph.D.
Primary Examiner

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